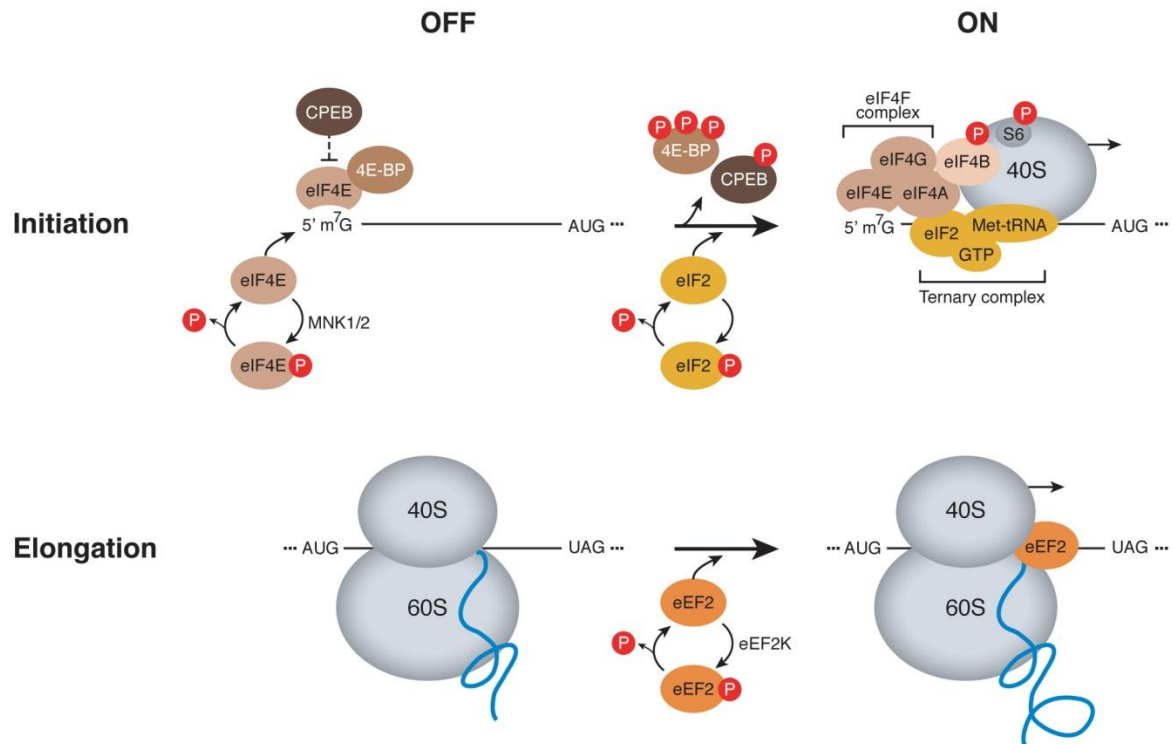


**Supplemental Figure 1.** Major regulatory events in cap-dependent translation.



Translational initiation (*top panel*) and translational elongation (*lower panel*) are kept under tight, coordinated control by signaling pathways that impinge upon eukaryotic initiation and elongation factors (eIFs and eEFs, respectively; *colored ovals*). See main text for details. Recognition of the 5' mRNA cap by eIF4E is required for initiation and leads to assembly of the eIF4F complex (eIF4E, eIF4G, eIF4A). A family of 4E-BPs inhibits this process by binding to eIF4E. A protein complex containing CPEB, an RNA-binding protein that blocks poly(A) tail addition, also inhibits eIF4F formation by binding eIF4E. Inhibition by 4E-BPs and the CPEB complex is relieved by phosphorylation (*red "P" circles*). Initiation is also facilitated by phosphorylation of eIF4B (to potentiate the RNA-helicase activity of eIF4A) and possibly S6. However, phosphorylation of eIF4E generally decreases eIF4E affinity for the cap and may function to reduce overall translation rates. Similarly, formation of the ternary complex (eIF2, Met-tRNA, and GTP) required to complete the 43S ribosomal complex is inhibited by phosphorylation of eIF2. During elongation, phosphorylation of eEF2 prevents its association with the ribosome and causes general translocation to stall. In some instances, this stalling allows translation of a subset of mRNAs. Small arrows indicate the direction of movement. Perpendicular lines indicate an inhibitory event. Curly blue lines represent ribosomally synthesized polypeptide chains that lengthen as translation proceeds. Abbreviations: AUG, initiation codon; 5' m<sup>7</sup>G, 5-prime 7-methylguanylate cap; ON, translation on; OFF, translation off; UAG, termination codon; 40S, small ribosomal subunit; 60S, large ribosomal subunit.